Appl. No. 09/936,291
Reply t Office Acti n of April 11, 2003

Attorn y Dockt: P67120US0

Amendments t the Specificati n:

Please replace the paragraph beginning at line 37 of page 11 with the following amended paragraph, in which the rephrased expression further specifies "astressin" as a corticotropin releasing factor (CRF) antagonist as well known in the art:

Suitable classes of antistress agents, including glucocorticoid inhibitors, corticotropin releasing hormone inhibitors, ACTH inhibitors, cholecystokinin inhibitors, benzodiazepines, gamma amino butyric acid potentiators, anti-glutaminergics and serotonergics amongst others. Preferred classes of antistress agents are pyridyl propanones including metyrapone, antiprogestins including mifepristone (RU 38486), and benzoylamino dipropylamino oxopentanoics including proglumide, and amino acids or peptides such as astressin which is a corticotropin releasing factor (CRF) antagonist, an amino acid peptide. Selection of an antistress agent can be made according to broad criteria such as animal species, age, and types of stress. It is noted that antiprogestins are contradicted for use in pregnant or conceiving animals.

Please replace the paragraph beginning at line 15 of page 12 with the following amended paragraph, in which a clerical error was corrected by adding a comma after astressin:

More generally, preferred antistress agents include metyrapone, mifepristone (RU 38486), astressin, CRH 9-41, proglumide, diazepam, allopregnanolone, dextromethorphan, zimelidine, vitamin C in combination with valine, leucine and isoleucine, and paroxetine but are not limited thereto. Combinations of two, three or more antistress agents with the same or different activity are also contemplated for use herein. Combinations with vitamin C and one or more of the amino acids valine, leucine and isoleucine are also provided. A preferred combination for nonpregnant and nonconceiving animals includes metyrapone and mifepristone (RU 38486). For pregnant or conceiving animals proglumide or astressin and metyrapone is currently suggested.

Please replace the paragraph beginning at line 34 of page 14 with the following amended paragraph, in which the clerical error in "pyrollopyrimidine" is corrected by using "pyrrolopyrimidine":

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The applicant also hypothesised that the effectiveness of the composition could be further enhanced through the use of a lipid membrane transfer facilitator, to assist the transfer of the therapeutic and antistress agents across cell membranes. This has proved to be the case. Compositions further including a lipid membrane transfer facilitator are therefore contemplated. Facilitators know in the art include pyrolidones such as N-methylpyrolidone, and pyrimidines such as pyrollopyrimidine pyrrolopyrimidine, amongst others. Preferred facilitators are pyrollopyrimidine and U-101033E (Also see Andreous P et al. J. Neuro Science Res., 47: 650-654 and Hall E et al 1995 Acta NeuroChir 66: 107-113 incorporated herein by reference). The concentration of the facilitator may be from 0.0000001 to 10% of the antistress agent component, preferably 0.01 to 0.1%

Please replace the paragraph beginning at line 21 of page 15 with the following amended paragraph, in which the clerical error in "pyrollopyrimidine" is corrected by using "pyrrolopyrimidine":

A typical composition for delivery could consist of 0.001% metyrapone, 0.01 % vitamin C, 0.0005% each valine, isoleucine and leucine, 0.0001% pyrollopyrimidine pyrrolopyrimidine, 5% glucose, 0.1% sodium benzoate and the remainder up to a 1L or 1 kg total coming from a carrier fluid or feed.

Please replace the paragraph beginning at line 10 of page 29 with the following amended paragraph, in which the clerical error in "pyrollopyrimidine" is corrected by using "pyrrolopyrimidine":

Adding a further compound, <u>pyrollopyrimidine pyrrolopyrimidine</u> to the mixture in a composition range of 0.0000001 to 10% of the metyrapone component further enhanced the effectiveness of the mixture. This is shown for sheep in Figure 14.

Please replace the paragraph beginning at line 20 of page 29 with the following amended paragraph, in which the clerical error in "pyrollopyrimidines" is corrected by using "pyrrolopyrimidine":

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In a further experiment similar to that described in experiments 3 and 4 the increased anthelmintic effect from vitamin C, isoleucine, valine and leucine alone or in combination with metyrapone, and metyrapone and pyrollopyrimidines—pyrrolopyrimidine was tested. Anthelmintics and these agents were given every four months and faecal count calculated each month in between treatments. Figure 15 demonstrates the results which clearly show that treatment with an anthelmintic and metyrapone is more effective than with the anthelmintic alone. The results were further enhanced by the addition of vitamin C, and the amino acids. Further increase in anthelmintic effect was seen when pyrollopyrimidine-pyrrolopyrimidine was added to the latter combination. By themselves, vitamin C and the amino acids had a small effect in increasing anthelmintic effectiveness.

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